AMENDMENTS TO THE CLAIMS

1. (Currently amended) A mouse targeting construct comprising:
   (a) a first polynucleotide sequence homologous to a target gene, wherein the target gene is a cGMP phosphodiesterase alpha subunit gene;
   (b) a second polynucleotide sequence homologous to the target gene; and
   (c) a selectable marker gene, wherein the selectable marker gene is located between the first and second polynucleotide sequences.
2. (Previously presented) The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker gene.
3. (Currently amended) A method of producing a mouse targeting construct, the method comprising:
   (a) obtaining a first polynucleotide sequence homologous to a cGMP phosphodiesterase alpha subunit gene;
   (b) obtaining a second polynuclotide sequence homologous to a cGMP phosphodiesterase alpha subunit gene;
   (c) providing a vector comprising a selectable marker gene; and
   (d) inserting the first and second sequences into the vector, to produce the targeting construct such that the selectable marker gene is located between the first and second sequences.
4. (Previously presented) A method of producing a mouse targeting construct, the method comprising:
   (a) providing a polynucleotide sequence homologous to a cGMP phosphodiesterase alpha subunit gene;
   (b) generating two different fragments of the polynucleotide sequence;
   (c) providing a vector having a gene encoding a selectable marker; and
   (d) inserting the two different fragments into the vector to form the targeting construct.
5. (Previously presented) A mouse embryonic stem cell comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, wherein the cell lacks production of functional cGMP phosphodiesterase alpha subunit protein and wherein a transgenic mouse

produced from the cell lacks production of functional cGMP phosphodiesterase alpha subunit protein and exhibits an eye abnormality or hyperactive behavior.

6. (Canceled)
7. (Canceled)
8. (Previously presented) A transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene wherein said mouse lacks production of functional cGMP phosphodiesterase alpha subunit protein and exhibits a phenotype comprising an eye abnormality.
9. (Previously presented) A cell obtained from the mouse of claim 8.
10. (Currently amended) A method of producing a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, the method comprising:
    (a) introducing the targeting construct of claim 1 into a mouse embryonic stem cell;
    (b) selecting for the mouse embryonic stem cell which has undergone homologous recombination;
    (c) introducing the cell selected for in step (b) into a blastocyst;
    (d) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said ~~pseudopregnant~~ mouse gives birth to a chimeric mouse; and
    (e) breeding the chimeric mouse to produce the transgenic mouse, wherein the transgenic mouse lacks production of functional cGMP phosphosdiesterase alpha subunit protein and comprises a phenotype comprising an eye abnormality or hyperactive behavior.
11. (Previously presented) A method of identifying an agent that ameliorates an abnormality associated with a homozygous disruption in a cGMP phosphodiesterase gene, the method comprising:
    (a) providing a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, wherein the mouse lacks production of functional cGMP phosphodiesterase alpha subunit protein and exhibits a phenotype comprising an eye abnormality; and
    (b) administering an agent to the transgenic mouse; and
    (c) determining whether the eye abnormality of the transgenic mouse is ameliorated.
12. (Canceled)
13. (Canceled)

14. (Canceled)
15. (Canceled)
16. (Canceled)
17. (Previously presented) The transgenic mouse of claim 8, wherein the eye abnormality is a retinal abnormality.
18. (Previously presented) The transgenic mouse of claim 17, wherein the retinal abnormality is characterized by retinal degeneration or retinal dysplasia.
19. (Previously presented) The transgenic mouse of claim 18, wherein the transgenic mouse exhibits an absence of photoreceptor layers.
20. (Previously presented) The transgenic mouse of claim 8, wherein the eye abnormality is consistent with vision problems or blindness.
21. (Previously presented) The transgenic mouse of claim 18, wherein the retinal abnormality is consistent with retinitis pigmentosa.
22. (Previously presented) The transgenic mouse of claim 8, wherein the eye abnormality comprises at least one of the following: thinning or vacuolation of the inner nuclear layer of the eye; thinning of the inner plexiform layer of the eye; loss of ganglion cell nuclei; gliosis of the nerve fiber layer; or attenuation of retinal vasculature.
23. (Currently amended) A method of producing a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, wherein the transgenic mouse comprises an eye abnormality phenotype, the method comprising:
    (a) introducing a cGMP phosphodiesterase alpha subunit gene targeting construct into a mouse embryonic stem cell;
    (b) selecting for the mouse embryonic stem cell which has undergone homologous recombination;
    (c) introducing the cell selected for in step (b) into a blastocyst;
    (d) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said ~~pseudopregnant~~ mouse gives birth to a chimeric mouse; and
    (e) breeding the chimeric mouse to produce the transgenic mouse comprising a homozygous disruption in an cGMP phosphodiesterase gene, wherein the transgenic mouse lacks production of functional cGMP phosphodiesterase protein and exhibits an eye abnormality phenotype.

24. (Canceled)

25. (Canceled)

26. (Canceled)

27. (Currently amended) A method of identifying an agent that ameliorates an ~~eye~~-abnormality associated with disruption of a cGMP phosphodiesterase gene, the method comprising:

    (a) administering an agent to the transgenic mouse of claim 8; and

    (b) determining whether the agent ameliorates the eye abnormality ~~of~~ in the transgenic mouse, wherein amelioration of the eye abnormality is indicative of an agent that ameliorates an abnormality associated with disruption of the cGMP phosphodiesterase gene.

28. (Previously presented) The method of claim 27, wherein the eye abnormality is a retinal abnormality.

29. (Previously presented) The method of claim 28, wherein the retinal abnormality is characterized by retinal degeneration or retinal dysplasia.

30. (Previously presented) The method of claim 29, wherein the transgenic mouse exhibits an absence of photoreceptor layers.

31. (Previously presented) The method of claim 27, wherein the eye abnormality comprises at least one of the following: thinning or vacuolation of the inner nuclear layer of the eye; thinning of the inner plexiform layer of the eye; loss of ganglion cell nuclei in the eye; gliosis of the nerve fiber layer of the eye; or attenuation of retinal vasculature in the eye.

32. (Canceled)

33. (Previously presented) A method of identifying an agent which modulates a phenotype comprising an eye abnormality, wherein the phenotype is associated with a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, the method comprising:

    (a) administering an agent to the transgenic mouse of claim 8; and

    (b) determining whether the agent modulates the phenotype comprising an eye abnormality.

34. (Canceled)

35. (Previously presented) A method of identifying an agent which modulates a phenotype associated with a disruption in an cGMP phosphodiesterase alpha subunit gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a homozygous disruption in an cGMP phosphodiesterase alpha subunit gene, wherein said mouse lacks production of functional cGMP phosphodiesterase protein and exhibits an eye abnormality or hyperactivity; and

(b) determining whether the agent modulates the eye abnormality or hyperactivity.

36. (Canceled)

37. (Canceled)

38. (Canceled)

39. (Canceled)

40. (Canceled)

41. (Canceled)

42. (Previously presented) A transgenic mouse comprising a homozygous disruption in an cGMP phosphodiesterase alpha subunit gene, wherein the transgenic mouse lacks production of functional cGMP phosphodiesterase protein and exhibits a phenotype comprising hyperactive behavior.

43. (Canceled)

44. (Canceled)

45. (Previously presented) A method of identifying an agent that ameliorates hyperactive behavior, the method comprising:

(a) administering an agent to the transgenic mouse of claim 42, and

(b) determining whether the agent ameliorates hyperactive behavior of the transgenic mouse.

46. (Canceled)

47. (Previously presented) A method of identifying an agent which modulates a phenotype associated with a disruption in a cGMP phosphodiesterase gene, the method comprising:

(a) administering an agent to the transgenic mouse of claim 42; and

(b) determining whether the agent modulates hyperactive behavior of the transgenic mouse.

48. (Canceled)